



Genomics and Systems Biology

LANL leads the world in computational finishing of microbial genomes

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In 2013, Los Alamos scientist Richard Sayre and his team genetically modified the organisms to harvest light more efficiently for maximum production.

Overview of Research and Highlights

Researchers at Los Alamos National Laboratory are using their renowned expertise in genomics, computation, and experimental biology as the foundation of a dynamic systems biology capability.

Systems biology examines biological components in an integrated fashion—genes, proteins, cells, communication networks, community constituents—and how their interactions give rise to the function and behavior of larger systems. Furthermore, incorporation of synthetic biology enables these systems to be improved.

The LANL portfolio includes sequencing, metabolomics, proteomics, transcriptomics, network analysis, computational modeling, and other methods that can be coupled tightly with experimental systems to both understand and predict their behavior.

This approach promises to enhance all aspects of biological research such as:

- Increasing the specificity of pathogen detection
- Designing more effective drugs through understanding the host-pathogen relationship
- Advancing plant and algal growth for bioenergy production
- Analyzing changes in the climate based on diverse microbial ecology

LANL has a rich history in genomic science – from the inception of the Human Genome Project and GenBank, to leading the world in computational finishing of microbial genomes and partnering with the DOE Joint Genome Institute.

Today, with rapidly advancing sequencing technology and the need for novel bioinformatics processes, our role continues to evolve and Los Alamos scientists are applying their expertise in sequencing and bioinformatics analysis toward challenges in bioenergy, pathogen detection, and microbial ecology.

In addition, scientists are developing new strategies to achieve these goals—such as experimental methods to isolate sufficient DNA from single cells and novel algorithms to help analyze metagenomes.

Los Alamos scientists also utilize other 'omics such as transcriptomics, proteomics, structural biology, and metabolomics. Coupled with cross-discipline expertise in sequencing, protein structure and function characterization, bioinformatics, and modeling with our national centers for stable isotopes, and flow cytometry, Los Alamos scientists are gaining a better understanding of relevant biological systems:

- Understanding the dynamics and treatments of viral diseases, such as HIV, influenza, and hepatitis.
- Explore the complex soil community of bacteria and fungi using metagenomic and transcriptomic approaches
- Designing computer models of the human immune system.
- Analyzing receptor-ligand interactions and cell signaling
- Examining host and pathogen response to infection
- Understanding the evolution of organisms in various systems
- Ascertaining protein function and dynamics, as well as protein folding.
- Using metabolomics to understand and impact plant growth

Advanced Experimental Methods

- Created NanoCluster Beacons that use a collection of a few atoms of silver as fluorescent reporters and are designed to bind with specific nucleic acid targets, such as pathogenic DNA. Reversible, inexpensive, and easy to use, NanoCluster Beacons are superior molecular probes that can be used to detect specific targets, such as influenza DNA or human oncogene (cancer) sequences, as well as play a crucial role in the study of sophisticated gene regulatory networks that could lead to a better understanding of cellular function. NanoCluster Beacons received an R&D 100 Award in 2011.
- Invented a rapid assay of protein folding by using the folding of a green fluorescent protein to monitor the folding of a test protein. It does this by linking the two proteins in a hybrid molecule with the characteristics of both. Applications include identifying the soluble proteins needed for medical research, drug discovery, chemical industrial process, and basic research into the structure and functions of proteins.
- Created “gel microdroplets,” to help scientists generate complete genomes from a single cell, thus opening the door to understanding the complex interrelationships of bacteria, viruses and eukaryotes that form “microbiome” communities in soil, in humans, and elsewhere in the natural world.

Big Data

- Developed Sequedex, a software package that performs the first step in analyzing the output of DNA sequencing instruments—classifying the organism the DNA likely came from and the metabolic function it likely carries out—faster, more sensitively, and more accurately than previously possible. Sequedex received an R&D 100 Award in 2012.
- Developed “BugBrowser,” a Java-based software project that provides highly flexible and dynamic visualization of the many features of viral, bacterial, and plasmid genomes. The tool can be used to visually compare multiple genomes, with an emphasis on gene similarity.

- Developing mathematical models of complex biological systems that play a role in cellular signaling. Developments include software such as BioNetGen (models biochemical networks inside cells) and EcoTFS (database that catalogs data regarding autoregulation of transcription factors in Escherichia coli).

Climate Change Research and Bioenergy Development

- Development of 'omics approaches to identify key soil bacterial and fungal populations in soil carbon cycling in forest and arid land ecosystems, (b) determination of genes and enzymes through which those populations process soil carbon, (c) the influence of anthropogenic N deposition on these processes, and (d) design of scalable molecular assays toward improved input for soil process models.
- Coupling algae sequence information with transcriptomics, proteomics, and metabolomics data to understand the biochemistry of high lipid production and to best inform decisions on feedstock choices for biofuel development

Genomics

- Proven expertise, and world leader in delivering high quality genome products and leading the field in generating libraries from low input DNA (including single cells)
- Developed workflows now used in production at major sequencing centers (e.g. JGI) to perform metagenome assembly for hundreds of projects
- Collaborating with the Centre for Chemical Biology at the Universiti Sains Malaysia on a human genome project to study achondroplasia disorder, the most common form of dwarfism. This work will provide clues to diagnose, treat, and prevent this and other genetic disorders.
- Working with the Kyrgyzstan Institute of Biotechnology to develop a genome database related to animal husbandry. The goals of this project are to define the genetic nature of commercial farm animals like sheep, identify opportunities to protect and preserve local indigenous breeds, and develop a genetic database for future selection of rare breeds for further research and commercial applications.
- Los Alamos was a key participant in the Human Genome Project. The goal of this project was to understand the genetic makeup of the human species and answer questions about human evolution, human interrelationships with other living things, and how humans differ from one another.

Capabilities

Bioinformatics and Analytics	Patrick Chain
Biomass and Diversity	David Fox
Biophysical Chemistry	Ryszard Michalczyk
Biophysics	Jim Werner
Computational Modeling	Sara Y. Del Valle
Detection and Diagnostics	Basil Swanson
Environmental Microbiology	Cheryl Kuske
Epidemiology	Ben McMahon
Genome Technologies	Tracy Erkkila
Molecular Recognition and Design	Andrew Bradbury
Pathogen Science	Elizabeth Hong-Geller
Pathogen Databases	Ben McMahon

- Los Alamos Genome Center: Coupled with our mission to serve the JGI, the Genome Center houses all of the newest sequencing technologies to deliver JGI projects as well as to many other sponsors, primarily focusing on sequencing critical pathogens and near neighbors, computational finishing and bioinformatics characterization of these pathogens, database and webservices for pathogen genome comparisons, metagenome sequencing and analysis for pathogen discovery and biosurveillance.
- [Center for Nonlinear Studies \(CNLS\)](#): The Center for Nonlinear Studies (CNLS) is an institutionally-supported center of excellence that conducts research in nonlinear and complex systems phenomena. One of its three research themes is Complexity in Biological and Bio-inspired Systems, including the emerging field of systems biology, with emphasis on modeling, computation, and theory.
- Stable Isotope Resource: This facility fosters the creation of new, efficient routes to synthesize stable isotopically labeled compounds. As such, the facility plays a valuable role in metabolomics for carbon sequestration and biodiesel production.
- [Protein Crystallography Station](#): This facility uses neutron diffraction techniques to perform groundbreaking work in better understanding enzyme structure and function, as well as elucidating the structure of cellulose (the building blocks of biomass). This information can be used in a multitude of ways, including the reduction of carbon emission in power plants and enhancing the production of algae-based biofuels.
- [National Flow Cytometry Resource](#): For over 30 years LANL has been a leader in the development and use of flow cytometry. Flow cytometry is useful for the sorting and analysis of algae cells for bioenergy, and the 2008 R&D 100-award winning acoustic flow cytometer inspired development of the Ultrasonic Biofuels Harvester, a 2010 R&D 100-award winner.

Partners

- [National Center for Systems Biology/The New Mexico Center for the Spatiotemporal Modeling of Cell Signaling](#): Los Alamos scientists are collaborating with this center under the leadership of the University of New Mexico's Cancer Center and Department of Pathology and in collaboration with Sandia National Laboratories and the University of New Mexico. The center's primary goal is to develop predictive models of cellular decision-making processes to better understand the causes of human disease and explore new treatment options. Diseases range from allergic reactions to various types of cancer.

Sponsors, Funding Sources, or Agencies

- Department of Energy Office of Biological and Environmental Research
- Department of Energy Office of Science
- National Institutes of Health
- Laboratory-Directed Research and Development
- Department of Homeland Security
- Defense Threat Reduction Agency/DoD

Awards

- 2012 R&D 100 Award for Sequedex
- 2011 R&D 100 Award for NanoCluster Beacons

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